

human FGF-21 MDSDETGFESGLWVSVLAGLLLGACQAHPIPDSSPLLQFG-GQV-RQRYLYTD 52
 ** * * * * * * ** * * * **
 mouse FGF-15 MARKWNGRAVARALVLATLWLAVS-GRPLAQ-QSQSVSDEDPLFLYGWGKITRLQYLYSA 58
 DAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYG 112
 * ** ** * ** ** * * * * * ** **
 GPYVSNCF LRIRSDGSVDCEEDQNERNLLEFRAVALKTIAIKDVSSVRYLCMSADGKIYG 118
 SLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPAPFLPLPGLPP 172
 * * *** *** * * * * * * *
 LIRYSEEDCTFREEMDCLGYNQYRSMKHLHIIFIQAK-PREQLQDQKPSNFIPVFHRSF 177
 ALPEPPGILAPQ--PPDVGSSDPLSMVGPSQG--RSPSYAS
 * * ** ** ***
 FETGDQLRSKMFSLPLESDSMDPFRMVEDVDHLVKSPSFQK

Fig. 1

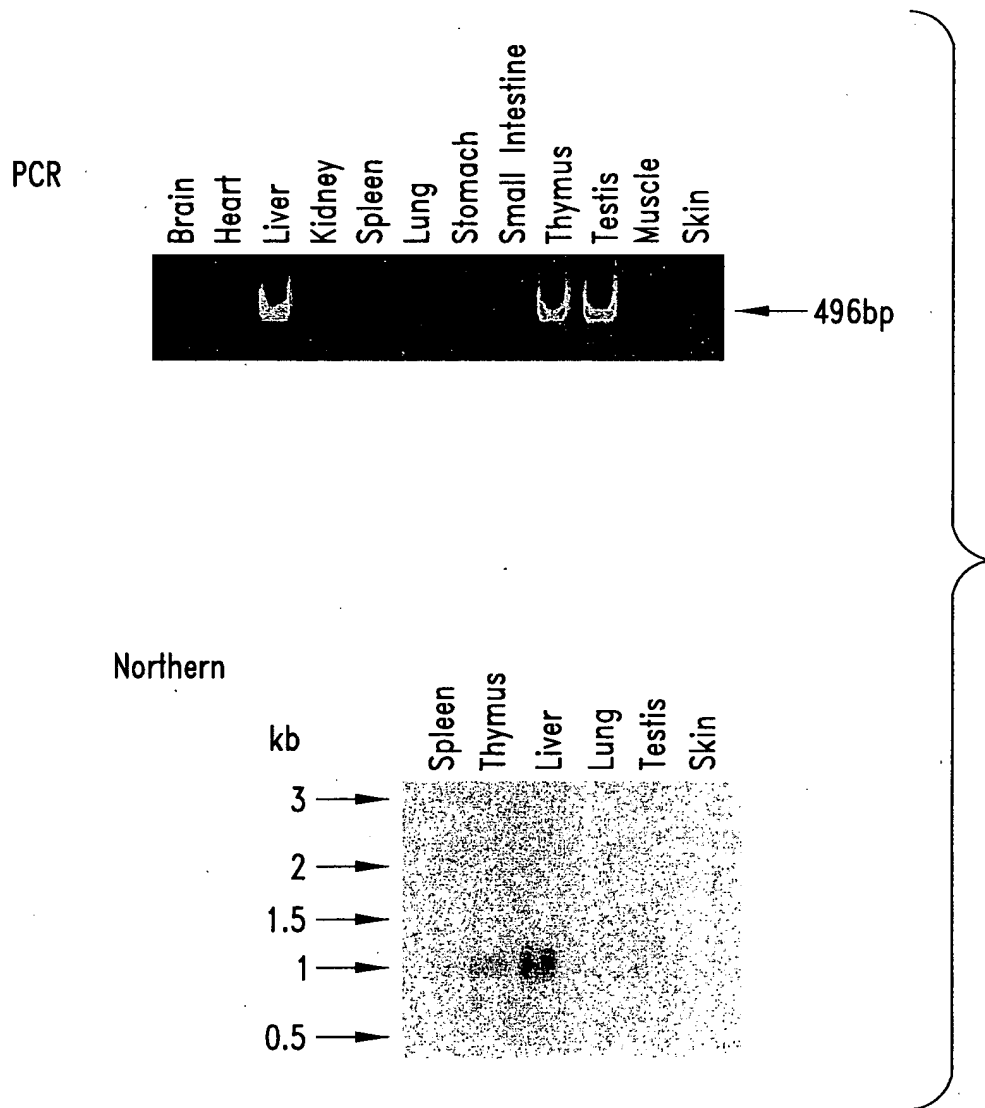
Human FGF-21	MDSDETGFHSGSLWVSVLAGLLG-ACQAHPIPDSPLLQF--GGQVRQRYLYTDDAQ-	56
	* **** * * * * *	
Human FGF-19	MMSGCVVHVW--ILAGLWLAVAGRPLAFSDAGPHVHYGWGDPRLRLHLYTSGPHGL	55
	TEAHLEIREDGTGGAADQSPESLLQLKALPGVIQILGVKTSRFLCQRPDGLYGSLLHF	116
	* ** * * * * * * * * *	
	SSCFLRIRADGVVDCARGQSAHSLLEIKAVALLRTVAIKGVHVSRYLCMGADGKMQGLLQY	115
	DPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPH--RDPAPRGPARFLPLPGLPPAL	174
	* * * * * * * * * *	
	SEEDCAFEELIRPDGYNVYRSEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEE	175
	PEP-PGILAPQ----PPDVGSSDPLSMV-GPSQGRSPSYAS	209
	** * * * * *	
	PEDLRGHLESDFSSPLETDSMDPFGLVTGLEAVRSPSFKEK	216

Fig. 2

Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PATENT

Express Mail No. EV064987286US

Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

*Fig. 3*

Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PR

Express Mail No. EV064987286US

Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

Filename: mouse FGF-21 cDNA in pGEM-T

Sequence Size: 659

Sequence Position: 1 - 659

Translation Position: 14 - 646

10 20 30 40 50 60
GAGCGCAGCCCTGATGGAATGGATGAGATCTAGAGTTGGGACCCTGGGACTGTGGGTCCG SEQ ID NO:1
M E W M R S R V G T L G L W V R SEQ ID NO:2

70 80 90 100 110 120
ACTGCTGCTGGCTGTCTTCTGCTGGGGGTCTACCAAGCATACCCATCCCTGACTCCAG
L L L A V F L L G V Y Q A Y P I P D S S

130 140 150 160 170 180
CCCCCTCCTCCAGTTTGGGGGTCAAGTCCGGCAGAGGTACCTCTACACAGATGACGACCA
P L L Q F G G Q V R Q R Y L Y T D D D Q

190 200 210 220 230 240
AGACACTGAAGCCACCTGGAGATCAGGGAGGATGGAACAGTGGTAGGCGCAGCACACCG
D T E A H L E I R E D G T V V G A A H R

250 260 270 280 290 300
CAGTCCAGAAAGTCTCCTGGAGCTCAAAGCCTTGAAGCCAGGGGTCAATCAAATCCTGGG
S P E S L L E L K A L K P G V I Q I L G

310 320 330 340 350 360
TGTCAAAGCCTCTAGGTTTCTTTGCCAACAGCCAGATGGAGCTCTCTATGGATCGCCTCA
V K A S R F L C Q Q P D G A L Y G S P H

370 380 390 400 410 420
CTTTGATCCTGAGGCCTGCAGCTTCAGAGAACTGCTGCTGGAGGACGGTTACAATGTGTA
F D P E A C S F R E L L L E D G Y N V Y

430 440 450 460 470 480
CCAGTCTGAAGCCCATGGCCTGCCCTGCGTCTGCCTCAGAAGGACTCCCCAAACCAGGA
Q S E A H G L P L R L P Q K D S P N Q D

490 500 510 520 530 540
TGCAACATCCTGGGGACCTGTGCGCTTCTGCCCATGCCAGGCCTGCTCCACGAGCCCCA
A T S W G P V R F L P M P G L L H E P Q

Fig. 4A

Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PRO

Express Mail No. EV064987286US

Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

550 560 570 580 590 600
AGACCAAGCAGGATTCCTGCCCCAGAGCCCCAGATGTGGGCTCCTCTGACCCCCTGAG
D Q A G F L P P E P P D V G S S D P L S

610 620 630 640 650 660
CATGGTAGAGCCTTTACAGGGCCGAAGCCCCAGCTATGCGTCCTGACTCTTCCTGAATC
M V E P L Q G R S P S Y A S *

Fig. 4B

Filename: human FGF-21 cDNA in pGEM-T

Sequence Size: 643

Sequence Position: 1 - 643

Translation Position: 9 - 638;

```

      10      20      30      40      50      60
agccattgatggactcggacgagaccgggttcgagcactcaggactgtgggtttctgtgc SEQ ID NO:3
      M D S D E T G F E H S G L W V S V L SEQ ID NO:4

      70      80      90     100     110     120
tggctggtcttctgctgggagcctgccaggcacacccccatccctgactccagtcctctcc
      A G L L L G A C Q A H P I P D S S P L L

      130     140     150     160     170     180
tgcaattcgggggccaagtccggcagcggtacctctacacagatgatgccagcagacag
      Q F G G Q V R Q R Y L Y T D D A Q Q T E

      190     200     210     220     230     240
aagcccacctggagatcagggaggatgggacggtggggggcgctgctgaccagagccccg
      A H L E I R E D G T V G G A A D Q S P E

      250     260     270     280     290     300
aaagtctcctgcagctgaaagccttgaagccgggagttattcaaactcttgggagtcaga
      S L L Q L K A L K P G V I Q I L G V K T

      310     320     330     340     350     360
catccagggtcctgtgccagcggccagatggggccctgtatggatcgctccactttgacc
      S R F L C Q R P D G A L Y G S L H F D P

      370     380     390     400     410     420
ctgaggcctgcagcttccgggagctgcttcttgaggacggatacaatgtttaccagtcgg
      E A C S F R E L L L E D G Y N V Y Q S E

      430     440     450     460     470     480
aagcccacggcctcccgtgcacctgccagggaacaagtccccacaccgggaccctgcac
      A H G L P L H L P G N K S P H R D P A P

      490     500     510     520     530     540
cccgaggaccagctcgcttctgccactaccaggcctgcccccgactcccggagccac
      R G P A R F L P L P G L P P A L P E P P
```

Fig. 5A

Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PRO

Express Mail No. EV064987286US

Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

550 560 570 580 590 600
ccggaatcctggccccccagcccccgatgtgggctcctcggaccctctgagcatggtgg
G I L A P Q P P D V G S S D P L S M V G

610 620 630 640 650
gaccttcccagggccgaagccccagctacgcttcctgaagcca
P S Q G R S P S Y A S *

Fig. 5B

human FGF-21 MDSDETGFEHSGLWVS-VLAGLLLGACQAHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEA 59
 * **** ** *** ** ***** * ***

mouse FGF-21 MEWMRSRVGTGLWVRLLLAVFLLGVYQAYPIPDSSPLLQFGGQVRQRYLYTDDDQDTEA 60

HLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGLYGSLLHFDPE 119
 ***** *** ***** ***** ***** ***** *****

HLEIREDGTVVGAHRSPESLLELKALKPGVIQILGVKASRFLCQQPDGLYGSPLHFDPE 120

ACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPALPEPPG 179
 ***** ** ** * ** **** *

ACSFRELLLEDGYNVYQSEAHGLPLRLPQKDSPNQDATSWGPVRFLPMPGLLHEPQDQAG 180

ILAPQPPDVGSSDPLSMVGPSQGRSPSYAS 209
 * * ***** * *****

FLPPEPPDVGSSDPLSMVEPLQGRSPSYAS 210

Fig. 6

Codon usage for yeast (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction	..
Gly	GGG	33.00	0.86	0.01	
Gly	GGA	70.00	1.82	0.02	
Gly	GGT	2672.00	69.62	0.91	
Gly	GGC	171.00	4.46	0.06	
Glu	GAG	277.00	7.22	0.10	
Glu	GAA	2442.00	63.63	0.90	
Asp	GAT	1100.00	28.66	0.48	
Asp	GAC	1211.00	31.55	0.52	
Val	GTG	117.00	3.05	0.04	
Val	GTA	75.00	1.95	0.03	
Val	GTT	1548.00	40.33	0.56	
Val	GTC	1026.00	26.73	0.37	
Ala	GCG	36.00	0.94	0.01	
Ala	GCA	203.00	5.29	0.06	
Ala	GCT	2221.00	57.87	0.65	
Ala	GCC	969.00	25.25	0.28	
Arg	AGG	20.00	0.52	0.01	
Arg	AGA	1336.00	34.81	0.83	
Ser	AGT	116.00	3.02	0.05	
Ser	AGC	94.00	2.45	0.04	
Lys	AAG	2365.00	61.62	0.78	
Lys	AAA	651.00	16.96	0.22	
Asn	AAT	347.00	9.04	0.22	
Asn	AAC	1259.00	32.80	0.78	
Met	ATG	766.00	19.96	1.00	
Ile	ATA	43.00	1.12	0.02	
Ile	ATT	1223.00	31.87	0.52	
Ile	ATC	1070.00	27.88	0.46	
Thr	ACG	28.00	0.73	0.01	

Fig. 7A

Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PROTEINS

Express Mail No. EV064987286US

Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

Thr	ACA	126.00	3.28	0.06
Thr	ACT	1129.00	29.42	0.50
Thr	ACC	962.00	25.07	0.43
Trp	TGG	325.00	8.47	1.00
End	TGA	10.00	0.26	0.09
Cys	TGT	254.00	6.62	0.89
Cys	TGC	33.00	0.86	0.11
End	TAG	11.00	0.29	0.10
End	TAA	85.00	2.21	0.80
Tyr	TAT	219.00	5.71	0.19
Tyr	TAC	913.00	23.79	0.81
Leu	TTG	2202.00	57.38	0.69
Leu	TTA	576.00	15.01	0.18
Phe	TTT	432.00	11.26	0.27
Phe	TTC	1145.00	29.83	0.73
Ser	TCG	26.00	0.68	0.01
Ser	TCA	149.00	3.88	0.06
Ser	TCT	1279.00	33.33	0.52
Ser	TCC	818.00	21.31	0.33
Arg	CGG	0.00	0.00	0.00
Arg	CGA	1.00	0.03	0.00
Arg	CGT	249.00	6.49	0.15
Arg	CGC	5.00	0.13	0.00
Gln	CAG	62.00	1.62	0.05
Gln	CAA	1225.00	31.92	0.95
His	CAT	236.00	6.15	0.35
His	CAC	433.00	11.28	0.65
Leu	CTG	52.00	1.35	0.02
Leu	CTA	236.00	6.15	0.07
Leu	CTT	90.00	2.35	0.03
Leu	CTC	14.00	0.36	0.00
Pro	CCG	10.00	0.26	0.01
Pro	CCA	1271.00	33.12	0.80
Pro	CCT	279.00	7.27	0.18
Pro	CCC	33.00	0.86	0.02

Fig. 7B

Codon usage for Drosophila (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction	..
Gly	GGG	6.00	0.28	0.00	
Gly	GGA	380.00	18.04	0.22	
Gly	GGT	575.00	27.29	0.34	
Gly	GGC	746.00	35.41	0.44	
Glu	GAG	1217.00	57.77	0.91	
Glu	GAA	115.00	5.46	0.09	
Asp	GAT	503.00	23.88	0.43	
Asp	GAC	654.00	31.04	0.57	
Val	GTG	719.00	34.13	0.45	
Val	GTA	29.00	1.38	0.02	
Val	GTT	226.00	10.73	0.14	
Val	GTC	608.00	28.86	0.38	
Ala	GCG	94.00	4.46	0.05	
Ala	GCA	80.00	3.80	0.04	
Ala	GCT	446.00	21.17	0.24	
Ala	GCC	1277.00	60.61	0.67	
Arg	AGG	48.00	2.28	0.06	
Arg	AGA	12.00	0.57	0.01	
Ser	AGT	16.00	0.76	0.01	
Ser	AGC	267.00	12.67	0.23	
Lys	AAG	1360.00	64.55	0.93	
Lys	AAA	108.00	5.13	0.07	
Asn	AAT	127.00	6.03	0.13	
Asn	AAC	878.00	41.67	0.87	
Met	ATG	387.00	18.37	1.00	
Ile	ATA	4.00	0.19	0.00	
Ile	ATT	390.00	18.51	0.29	
Ile	ATC	969.00	45.99	0.71	

Fig. 8A

Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PRO

Express Mail No. EV064987286US

Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

Thr	ACG	114.00	5.41	0.08
Thr	ACA	34.00	1.61	0.02
Thr	ACT	164.00	7.78	0.11
Thr	ACC	1127.00	53.49	0.78
Trp	TGG	243.00	11.53	1.00
End	TGA	1.00	0.05	0.01
Cys	TGT	20.00	0.95	0.08
Cys	TGC	220.00	10.44	0.92
End	TAG	12.00	0.57	0.17
End	TAA	58.00	2.75	0.82
Tyr	TAT	113.00	5.36	0.16
Tyr	TAC	574.00	27.25	0.84
Leu	TTG	210.00	9.97	0.12
Leu	TTA	9.00	0.43	0.01
Phe	TTT	62.00	2.94	0.09
Phe	TTC	635.00	30.14	0.91
Ser	TCG	195.00	9.26	0.17
Ser	TCA	29.00	1.38	0.02
Ser	TCT	103.00	4.89	0.09
Ser	TCC	558.00	26.49	0.48
Arg	CGG	7.00	0.33	0.01
Arg	CGA	25.00	1.19	0.03
Arg	CGT	281.00	13.34	0.34
Arg	CGC	465.00	22.07	0.55
Gln	CAG	703.00	33.37	0.91
Gln	CAA	66.00	3.13	0.09
His	CAT	88.00	4.18	0.22
His	CAC	312.00	14.81	0.78
Leu	CTG	1182.00	56.10	0.69
Leu	CTA	21.00	1.00	0.01
Leu	CTT	55.00	2.61	0.03
Leu	CTC	224.00	10.63	0.13
Pro	CCG	84.00	3.99	0.09
Pro	CCA	135.00	6.41	0.15
Pro	CCT	72.00	3.42	0.08
Pro	CCC	626.00	29.71	0.68

Fig. 8B

Codon usage for enteric bacterial (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction . .
Gly	GGG	13.00	1.89	0.02
Gly	GGA	3.00	0.44	0.00
Gly	GGU	365.00	52.99	0.59
Gly	GGC	238.00	34.55	0.38
Glu	GAG	108.00	15.68	0.22
Glu	GAA	394.00	57.20	0.78
Asp	GAU	149.00	21.63	0.33
Asp	GAC	298.00	43.26	0.67
Val	GUG	93.00	13.50	0.16
Val	GUA	146.00	21.20	0.26
Val	GUU	289.00	41.96	0.51
Val	GUC	38.00	5.52	0.07
Ala	GCG	161.00	23.37	0.26
Ala	GCA	173.00	25.12	0.28
Ala	GCU	212.00	30.78	0.35
Ala	GCC	62.00	9.00	0.10
Arg	AGG	1.00	0.15	0.00
Arg	AGA	0.00	0.00	0.00
Ser	AGU	9.00	1.31	0.03
Ser	AGC	71.00	10.31	0.20
Lys	AAG	111.00	16.11	0.26
Lys	AAA	320.00	46.46	0.74
Asn	AAU	19.00	2.76	0.06
Asn	AAC	274.00	39.78	0.94
Met	AUG	170.00	24.68	1.00
Ile	AUA	1.00	0.15	0.00
Ile	AUU	70.00	10.16	0.17
Ile	AUC	345.00	50.09	0.83
Thr	ACG	25.00	3.63	0.07
Thr	ACA	14.00	2.03	0.04
Thr	ACU	130.00	18.87	0.35

Fig. 9A

Title: HUMAN FGF-21 GENE AND GENE EXPRESSION PRODUCTS

Express Mail No. EV064987286US

Inventor(s): Nobuyuki Itoh et al. Serial No. 10/060,765 Docket No. PP-16758.003/201130.408D1

AmAcid	Codon	Number	/1000	Fraction . .
Thr	ACC	206.00	29.91	0.55
Trp	UGG	55.00	7.98	1.00
End	UGA	0.00	0.00	0.00
Cys	UGU	22.00	3.19	0.49
Cys	UGC	23.00	3.34	0.51
End	UAG	0.00	0.00	0.00
End	UAA	0.00	0.00	0.00
Tyr	UAU	51.00	7.40	0.25
Tyr	UAC	157.00	22.79	0.75
Leu	UUG	18.00	2.61	0.03
Leu	UUA	12.00	1.74	0.02
Phe	UUU	51.00	7.40	0.24
Phe	UUC	166.00	24.10	0.76
Ser	UCG	14.00	2.03	0.04
Ser	UCA	7.00	1.02	0.02
Ser	UCU	120.00	17.42	0.34
Ser	UCC	131.00	19.02	0.37
Arg	CGG	1.00	0.15	0.00
Arg	CGA	2.00	0.29	0.01
Arg	CGU	290.00	42.10	0.74
Arg	CGC	96.00	13.94	0.25
Gln	CAG	233.00	33.83	0.86
Gln	CAA	37.00	5.37	0.14
His	CAU	18.00	2.61	0.17
His	CAC	85.00	12.34	0.83
Leu	CUG	480.00	69.69	0.83
Leu	CUA	2.00	0.29	0.00
Leu	CUU	25.00	3.63	0.04
Leu	CUC	38.00	5.52	0.07
Pro	CCG	190.00	27.58	0.77
Pro	CCA	36.00	5.23	0.15
Pro	CCU	19.00	2.76	0.08
Pro	CCC	1.00	0.15	0.00

Fig. 9B